IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

ON APPEAL FROM THE PRIMARY EXAMINER TO THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application No.	:	10/736,489
Applicants	:	Xia Zhao et al.
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Title	:	Terminal Sterilization of Prefilled Containers
Group Art Unit	:	1744
Examiner	:	Monzer R. Chorbaji
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MAIL STOP APPEAL BRIEF – PATENTS
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

APPELLANTS' BRIEF UNDER 37 C.F.R. § 41.37

Sir:

The present Appeal Brief is submitted in support of the Notice of Appeal filed August 9, 2006, and received August 14, 2006 by the United States Patent and Trademark Office. Filed concurrently herewith is a Petition for One-Month Extension of Time.

I hereby certify that this correspondence is being deposited with the United States Postal Service as First Class Mail in an envelope addressed to Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on November 9, 2006.

Lisa R. McNany
(Name of Person Mailing Paper or Fee)

Signature 11/09/2006 Date

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(i) REAL PARTY IN INTEREST

The real party in interest for the application in this Appeal is assignee Becton, Dickinson and Company, by virtue of the Assignment dated December 4, 2003, recorded at Reel/Frame 014809/0316 on December 15, 2003 in the United States Patent and Trademark Office.

(ii) RELATED APPEALS AND INTERFERENCES

As the legal representative of Appellants, the undersigned attorney has no knowledge of any appeals or interferences directly related to this Appeal.

(iii) STATUS OF CLAIMS

Claims 1-6, 8-52 and 54-56 are presently pending in the application, and are reproduced in the Appendix attached hereto. Claims 1, 17, 32 and 55 are presented in independent form.

In a final Office Action dated April 19, 2006, claims 1-3, 8, 12-13, 16-18, 21-22, 24-25, 28-34, 36-38, 42-43 and 46-51 were finally rejected under 35 U.S.C. §102(b) as allegedly being anticipated by U.S. Patent No. 6,231,936 to Kozimor et al. ("Kozimor"). Claims 6-7 and 52-55 were finally rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Kozimor and further in view of the admitted state of the prior art. Claims 4-5, 23 and 35 were finally rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Kozimor and further in view of Jacobs et al. (Acta Pharm, IDS) ("Jacobs"). Claims 9, 14-15, 26, 39 and 44-45 were finally rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Kozimor and further in view of U.S. Patent No. 4,994,552 to Williams et al. ("Williams"). Claims 10-11, 27 and 40-41 were finally rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Kozimor and further in view of U.S. Patent No. 6,437,048 to Saito et al. ("Saito"). Claims 19-20 were finally rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Kozimor and further in view of U.S. Patent No. 6,123,900 to Vellutato ("Vellutato").

An Amendment After Final was filed on June 19, 2006 in response to the final Office Action, in which claims 1, 17 and 32 were amended to include the language recited in claims 7 and 53, and claims 7 and 53 were therefore cancelled.

In an Advisory Action dated July 5, 2006, the claim amendments were entered, however the application was not allowed. Instead, independent claims 1, 17 and 32 were identified as rejected in a similar manner as claim 55 was previously rejected in the final Office Action (i.e., under 35 U.S.C. §103(a) as being unpatentable over Kozimor and further in view of the admitted state of the prior art), and dependent claims 2-3, 6, 8, 12-13, 16, 18, 21-22, 24-25, 28-31, 33-34, 36-38, 42-43, 46-52 and 54-56 were identified as being "rejected as shown on pages 2-5 of the final Office Action".

Accordingly, *all of the independent claims, namely claims 1, 17, 32 and 55, stand rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Kozimor and further in view of the admitted state of the prior art.*

Further, since the amended claim language incorporates into independent claims 1, 17 and 32 the language of dependent claims 7 and 53 (which were previously rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Kozimor and further in view of the admitted state of the prior art), and since these amended independent claims are indicated as rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Kozimor and further in view of the admitted state of the prior art, *dependent claims 2-3, 6, 8, 12-13, 16, 18, 21-22, 24-25, 28-31, 33-34, 36-38, 42-43, 46-52 and 54-56 therefore also stand rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Kozimor and further in view of the admitted state of the prior art.*

Dependent claims 4-5, 23 and 35 stand rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Kozimor and further in view of Jacobs in combination with the admitted state of the prior art.

Dependent claims 9, 14-15, 26, 39 and 44-45 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Kozimor and further in view of Williams in combination with the admitted state of the prior art.

Dependent claims 10-11, 27 and 40-41 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Kozimor and further in view of Saito in combination with the admitted state of the prior art.

Dependent claims 19-20 stand rejected as being unpatentable over Kozimor and further in view of Vellutato in combination with the admitted state of the prior art.

(iv) STATUS OF AMENDMENTS

In a final Office Action dated April 19, 2006, all of claims 1-55 were rejected. As noted above, an Amendment after Final Rejection was filed on June 19, 2006, including amendments to independent claims 1, 17 and 32 to include the subject matter of claims 7 and 53, namely that the medium contained in the prefilled container contains less than about 3.4 ppm of oxidizable substances, and claims 7 and 53 were cancelled. Additionally, the dependencies of dependent claims 52 and 54 were amended, and new dependent claim 56 was added to include similar language as that set forth in pending claims 52 and 54.

In response, an Advisory Action was issued on July 5, 2006, entering the amendments to the claims, but indicating that the Amendment After Final did not place the application in condition for allowance. Appellants thereafter timely filed a Notice of Appeal on August 9, 2006, with the present Brief being filed in support of the Appeal.

(v) SUMMARY OF CLAIMED SUBJECT MATTER

The invention is generally directed to methods for inhibiting adverse reaction of the contents of a container that has been subjected to a radiation sterilization treatment, as well as to sterilized articles including containers that have been subjected to a radiation sterilization treatment, with a medium contained within the container having pharmacologically acceptable properties.

Independent claim 1 is specifically directed to a method for inhibiting adverse reaction of the contents of a container that is subjected to a radiation sterilization procedure. The method comprises providing a container made of a composition comprising a polyolefin material and a radiation stabilizer, and prefilling the container with a medium prior to subjecting the container to a gamma irradiation sterilization treatment, with the medium including less than about 3.4 ppm of oxidizable substances after radiation sterilization. Such language is clearly described in the specification at paragraph [0007], [0008] and [0029] of the application as originally filed.

Independent claim 17 is specifically directed to a method of sterilizing a prefilled container. The method comprises providing a container made of a composition comprising a polyolefin material and a radiation stabilizer, filling the container with a medium, and irradiating the container filled with the medium with gamma irradiation, wherein the medium includes less than about 3.4 ppm of oxidizable substances after the irradiating step. Such language is also described in the specification at paragraph [0007], [0008] and [0029] of the application as originally filed.

Independent claim 32 is specifically directed to a sterilized article. The article comprises a container made of a composition comprising a polyolefin material and a radiation stabilizer, and a medium contained within the container, which medium includes less than about 3.4 ppm of oxidizable substances, wherein the container containing the medium has been subjected to a gamma irradiation sterilization treatment after being filled with the medium. Such language is set forth at paragraphs [0011] and [0031] of the specification as originally filed.

Independent claim 55 is specifically directed to a sterilized article comprising a container and a medium contained within the container, wherein the container containing the medium has been subjected to a gamma irradiation sterilization treatment after being

filled with the medium, and wherein the medium includes less than about 3.4 ppm of oxidizable substances after the irradiating step. Such language is also set forth at paragraphs [0011] and [0031] of the specification as originally filed.

(vi) GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

The issues on appeal include:

I. Whether Kozimor, considered alone or in combination with the admitted state of the prior art, teaches or suggests that prefilling a container prior to a gamma radiation sterilization treatment, inhibits adverse reaction of the contents of the container?

(vii) ARGUMENT

A. KOZIMOR, WHETHER CONSIDERED ALONE OR IN COMBINATION WITH THE ADMITTED STATE OF THE PRIOR ART, FAILS TO TEACH OR SUGGEST THAT PREFILLING A CONTAINER PRIOR TO A GAMMA RADIATION STERILIZATION TREATMENT INHIBITS ADVERSE REACTION OF THE CONTENTS OF THE CONTAINER.

Radiation sterilization of polyolefin materials causes a degradation of the container material, which can adversely affect the properties of a medium contained within a container. The present invention is generally directed to the unexpected and surprising finding that the radiation sterilization of a container constructed of a polyolefin material that includes a radiation stabilizer will have less of an adverse impact on the contents of the container if the container is prefilled with a medium prior to subjecting the container to a gamma radiation treatment, such that the medium contained within the container will exhibit pharmacologically acceptable properties.

In particular, it is well known to construct containers useful as medical devices, and particularly syringes, out of polyolefin materials. Polyolefin is particularly useful in such applications due to its ease of manufacture and inexpensive raw materials. However, polyolefin materials such as polypropylene are not very resistant to the softening effects and the degradation that occurs when such materials are subjected to sterilizing dosages of ionizing radiation, particularly gamma radiation. As a result, irradiation of polyolefin containers causes the generation of highly reactive species. Such species can alter the contents of the container, and through the present invention it has been discovered that the generation of these species can be inhibited in order to prevent degradation of the medium contained within the container in order to meet the European and/or U.S. Pharmacopoeia requirements for such media.

More particularly, the present invention provides the unexpected finding that the integrity of a medium contained within a container can be maintained within an acceptable useful range, with the level of oxidizable substances within the medium maintained below about 3.4 ppm, by using radiation stable polyolefins in combination with gamma irradiation, and by ensuring that the container is filled with the medium prior to such

gamma irradiation treatment. The present inventors have discovered that a synergy exists between the composition of the container, the type of sterilization treatment such as gamma irradiation, and the requirement that a medium be present within the container prior to the gamma irradiation. Specifically, it has now been discovered that prefilling the container prior to irradiation provides a medium to neutralize the radical reactions during irradiation, thus minimizing the reactions which incorporate radical scavengers, i.e., oxidizable substances, such as hydrogen peroxide. In other words, the present invention provides a useful product by inhibiting any adverse reaction of the contents of the prefilled container during radiation sterilization treatment from occurring.

1. The Rejection

The Examiner contends that Kozimor teaches radiation stable prefilled syringes that are to be sterilized by gamma irradiation, and that the prefilled syringes include polyolefin material and a radiation sterilizer. (Final Office Action at para.2, p. 2). The Examiner further contends that the syringes of Kozimor may be prefilled, such that "irradiating" necessarily refers to irradiation of syringes that have already been sealed prior to the irradiating step. (Final Office Action at para.2, p. 2). The Examiner recognizes that "Kozimor fails to teach placing medium irradiation limitations on ultraviolet absorbance at certain wavelength range value and on the concentration of hydrogen peroxide". (Final Office Action at para.6, p. 4). The Examiner contends, however, that the specification teaches that the required UV absorbance level that the presence of oxidizing agents should be below 3.4 ppm after the process of irradiation and concludes that it would have been obvious to "modify the method of the Kozimor reference to include limits on UV absorbance value and on hydrogen peroxide value in order to comply with the European and/or U.S. Pharmacopoeia guidelines as taught in the specification." (Final Office Action at para.2, p. 2).

Kozimor, however, fails to teach or even suggest that the contents of a container may be affected based on whether the container is filled or unfilled prior to a gamma radiation treatment.

2. No *Prima Facie* Case of Obviousness Under 35 U.S.C. § 103(a)

In order to establish a *prima facie* case of obviousness, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one skilled in the art, to modify the reference or combine reference teachings, and there must be a reasonable likelihood of success in doing so. *See* MPEP § 2143. An obviousness rejection is proper only if the prior art, coupled with the knowledge generally available at the time of the invention, contained some suggestion or incentive that would have motivated the skilled artisan to combine the references and that there would be a reasonable expectation of success in doing so. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991); *See also Karsten Mfg. Corp. v. Cleveland Gulf Co.*, 242 F.3d 1376, 1385, 58 USPQ2d 1286, 1293 (Fed. Cir. 2001); *McGinley v. Franklin Sports, Inc.*, 262 F.3d 1339, 1351, 60 USPQ2d 1001, 1008 (Fed. Cir. 2001) ("To prevent hindsight invalidation of patent claims, the law requires some 'teaching, suggestion or reason' to combine cited references.").

Kozimor fails to teach or suggest that the contents of a container may be affected through radiation sterilization based on whether the container is filled or unfilled prior to gamma radiation treatment. Nothing in Kozimor even remotely suggests that prefilling the container prior to radiation treatment will have any effect on the medium within the container. In rejecting the claims, the Examiner contends in the Advisory Action that "Kozimor explicitly teaches that prefilled containers will undergo gamma irradiation sterilization step", and that "the benefit of maintaining oxidizable substances after radiation to below 3.4 ppm is disclosed in the admitted state of the prior art...".

The Examiner fails to demonstrate, however, how one of ordinary skill in the art, upon reading Kozimor and the Pharmacopoeia requirements, would recognize that preventing the concentration of oxidizable substances to below 3.4 ppm after gamma radiation treatment could be achieved by pre-filling the container. There is no explanation by the Examiner as to how one skilled in the art would recognize how to achieve the benefit of maintaining the oxidizable substances below such a limit based merely on the teachings of Kozimor and the knowledge that it is desirable to maintain the oxidizable substances at a reduced level. Indeed, Kozimor does not even distinguish between sterilization methods and fails to even recognize that the type of sterilization, or whether the container is filled or empty prior to sterilization, could have any affect whatsoever on such properties.

Moreover, the teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in Appellant's disclosure. *In re Vaeck.* The mere fact that the Pharmacopoeia standards require a certain property does not correct the deficient teachings of Kozimor. There is nothing in Kozimor which would lead one skilled in the art to recognize that filling the container prior to subjecting it to gamma radiation will reduce the level of oxidizable substances. In fact, Kozimor discloses that the syringes taught therein can be filled either before or after irradiation. See Kozimor, col. 4, lines 13-15. Such teachings do not provide any reasonable expectation that filling the container prior to a gamma radiation treatment will successfully reduce the oxidizable substances when compared with a similar treatment to a container which is not filled. Because there is no suggestion or motivation to modify or combine references in such a way, or more directly that there would be success in doing so, there is a clear deficiency in the *prima facie* case in support of this rejection.

3. Kozimor Teaches Away From the Present Invention

In fact, by disclosing that the syringes can be filled either before or after irradiation, Kozimor actually teaches away from the present invention. When considering a reference, it is necessary to consider those portions of the reference that teach away from the claimed invention. *Bausch & Lomb, Inc. v. Barnes-Hind/Hydrocurve, Inc.*, 796 F.2d 443, 230 USPQ 416 (Fed. Cir. 1986). When interpreting the patentability of a claim, the law requires that a reference be considered for all of its teachings, including disclosure that diverges and teaches away from the invention at hand as well as disclosures that point toward and teach the invention. *In re Dow Chem. Co.*, 837 F.2d 469, 5 USPQ2d 1529 (Fed. Cir. 1988). It has been discovered through the present invention that filling the container prior to irradiation reduces the level of oxidizable substances within the medium, when compared to a container which is filled after the container has been irradiated. Kozimor, however, fails in any way to recognize such a distinction, and in fact teaches that sterilization can be accomplished by irradiating before or after filling the container. Such teachings are entirely contrary to the present invention, and specifically teach away from the present discovery that a pharmacologically acceptable product can be maintained by pre-filling the syringe prior to such treatment.

4. The Results of the Present Invention are Unexpected

Furthermore, one way for an applicant to rebut an allegation of obviousness is to make a showing of "unexpected results," i.e., to show that the claimed invention exhibits some superior property or advantage that a person of ordinary skill in the relevant art would have found surprising or unexpected. *In re Soni*, 54 F.3d 746, 750, 34 USPQ2d 1684, 1687 (Fed. Cir.1995). The discovery of the present invention that filling the container prior to irradiation treatment reduces the level of oxidizable substances within the medium, when compared to a container which is filled after the container has been irradiated, is an unexpected result. The comparative data set forth in Examples 3 and 4 of the present application set forth such unexpected results. Example 3 demonstrates the unexpected result that when syringes, constructed of a radiation stable polyolefin polymer, are pre-filled with a sample medium prior to the irradiation step, there is a marked improvement in sample quality when compared to syringes which were irradiated and then filled. Example 4 demonstrates that the type of radiation treatment in a terminal sterilization process is important to product quality because gamma irradiation reduces the amount of oxidizable materials in a sample to a greater extent than E-beam irradiation.

The Examiner has failed to demonstrate how such a result would be expected based on the prior art. In fact, Kozimor notes that sterilization of syringes can be accomplished with the syringe being filled or unfilled, without any differentiation between the two processes. Based on such a disclosure in the prior art, one skilled in the art would have no expectation that filling the syringe prior to a gamma radiation treatment would provide a markedly improved product with reduced oxidizable substances let alone a product with less than about 3.4 ppm of oxidizable substances. Clearly the product which has been pre-filled prior to being subjected to a gamma radiation treatment exhibits a superior property, as demonstrated through Examples 3 and 4 as noted. Such a superior property is unexpected based on the limited teachings of Kozimor, and therefore rebuts any allegation of obviousness based on Kozimor, whether considered alone or in combination with the recognition that it is desirable to provide a medium with a reduced level of oxidizable substances.

The Examiner fails to identify where in the references it is suggested that the irradiation treatment should occur only after the container is filled, and that doing so will successfully result in a reduction in the oxidizable substances present within the medium. As

previously noted, Kozimor teaches away from this suggestion by allowing for syringes to be filled before or after sterilization without suggesting that one option is more desirable than the other. The Examiner also fails to identify any evidence in the reference that would suggest to one skilled in the art that the type of radiation treatment has an effect on the amount of oxidizable materials in the sample, as now discovered through the present invention. This synergistic effect is realized only through the present invention through the specific sterilization treatment with the container filled in a specific manner. The existence of standard Pharmacopoeia requirements does nothing to cure these deficiencies, but instead only suggests the desirability of maintaining a low level of such substances. The Examiner fails to indicate why one skilled in the art, having knowledge of these requirements, would know to modify the Kozimor teachings in such a way that the polyolefin containers taught therein would undergo gamma radiation only after being filled with a medium and that doing so would successfully inhibit the adverse reactions on the enclosed medium so that the level of oxidizable substances in the medium is below 3.4 ppm. Such results are shown to be surprising and unexpected, particularly based on the teachings in Kozimor that syringes can be radiation sterilized either before or after filling, whereas the present invention has surprisingly discovered that the syringe must in fact be pre-filled to achieve a product with less than 3.4 ppm oxidizable substances.

The additional references cited by the Examiner merely relate to features of the dependent claims. Jacobs is directed to the use of gamma radiation for the sterilization of water for injections and normal saline solution for injection, and is cited merely for its alleged teachings of the use of gamma irradiation of saline water and, for example, a pH of 5.0 for saline water after gamma irradiation.

Williams is directed to a high clarity polymeric composition which is stable toward sterilizing radiation, and is cited merely for allegedly teaching a composition of a container which includes a clarifying agent such as dibenzylidene sorbitol alkyl thioether, a mobilizing additive such as hydrocarbon oil and the stabilizer bis (4-piperidinyl) diester of a dicarboxlic acid.

Saito is directed to a plastic molded product using a resin composition with polypropylene as the main component, and is cited merely as a teaching of the use of aluminum 2,2'-methylene-bis(4,6-di-t-butylphenol) phosphate.

Vellutato is directed to a method of sterilizing chemical compositions utilizing irradiation techniques which allow for the chemical composition being sterilized to be maintained for extended periods of time, and it is cited merely for allegedly teaching irradiating pharmaceutical compositions after being packaged inside a carton with gamma irradiation.

None of the references add anything further to the deficiencies of Kozimor. Moreover, there is nothing in any of these references to suggest the desirability of pre-filling prior to gamma sterilization.

Based on these remarks, a *prima facie* case of obviousness of the claims has not been made because the Examiner has failed to establish any suggestion or motivation to modify or combine Kozimor with any of the prior art teachings which would render the present invention obvious, or that there would be a reasonable likelihood of success in doing so. The rejection of independent claims 1, 17, 32 and 55 based on the combination of Kozimor and the admitted state of the prior art should therefore be overturned.

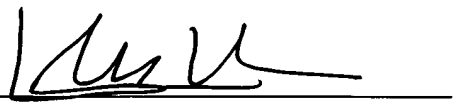
Furthermore, in view of the failure of the secondary references to cure the deficiencies of Kozimor taken with the admitted state of prior art and because all of dependent claims 2-6, 8-16, 18-31, 33-52, 54 and 56 depend either directly or indirectly from one of these independent claims, their rejections also should be overturned.

CONCLUSION

Having set forth factual and legal bases which support the patentability of the claims on appeal, all of claims 1-6, 8-52 and 54-56 are allowable. Accordingly, Appellants respectfully urge the Board to reverse the Examiner's final rejection of the claims.

Respectfully submitted,

THE WEBB LAW FIRM

By 

Kirk M. Miles
Registration No. 37,891
Attorney for Appellant
700 Koppers Building
436 Seventh Avenue
Pittsburgh, Pennsylvania 15219
Telephone: 412-471-8815
Facsimile: 412-471-4094
E-mail: webblaw@webblaw.com

(viii) CLAIMS APPENDIX

1. A method for inhibiting adverse reaction of the contents of a container subjected to a radiation sterilization procedure comprising:

providing the container made of a composition comprising a polyolefin material and a radiation stabilizer; and

prefilling the container with a medium prior to subjecting the container to a gamma irradiation sterilization treatment, wherein said medium includes less than about 3.4 ppm of oxidizable substances after radiation sterilization.

2. A method as in claim 1, wherein the medium is selected from the group consisting of a therapeutic fluid and a non-therapeutic fluid.

3. A method as in claim 2, wherein the medium comprises a drug for parenteral administration to the body.

4. A method as in claim 2, wherein the medium comprises saline water.

5. A method as in claim 1, wherein the medium has a pH between about 4.5 and about 7.0 after radiation sterilization.

6. A method as in claim 1, wherein the medium exhibits ultraviolet absorbance of less than about 0.2 at a wavelength between 220 and 340 nm.

7. (Cancelled)

8. A method as in claim 1, wherein the container is manufactured from a composition comprising a polyolefin, a mobilizing amount of a liquid mobilizer compatible with said polyolefin, and a radiation stabilizing amount of a hindered piperidine stabilizer.

9. A method as in claim 8, wherein the composition of the container further comprises a clarifying amount of a dibenzylidene sorbitol alkyl thioether clarifier.

10. A method as in claim 8, wherein the composition of the container further comprises a nucleating agent comprising a 2,2'-methylene-bis(4,6-di-t-butylphenol)phosphate salt.

11. A method as in claim 10, wherein the 2,2'-methylene-bis(4,6-di-t-butylphenol)phosphate salt is selected from the group consisting of sodium 2,2'-methylene-bis(4,6-di-t-butylphenol)phosphate and aluminum 2,2'-methylene-bis(4,6-di-t-butylphenol) phosphate.

12. A method as in claim 8, wherein the composition of the container further comprises about 0.1 to 10% of an additional polymer.

13. A method as in claim 8, wherein the polyolefin is selected from the group consisting of polyethylene, polypropylene, polymethylpentene, polytetrafluoroethylene and copolymers thereof.

14. A method as in claim 8, wherein the mobilizing additive is selected from the group consisting of a hydrocarbon oil, phthalic ester oil, polymer grease, vegetable oil, mineral oil and silicone oil.

15. A method as in claim 8, wherein the stabilizer is a bis(4-piperidinyl) diester of a dicarboxylic acid.

16. A method as in claim 1, where the gamma irradiation ranges from about 10 kGy to about 60 kGy.

17. A method of sterilizing a prefilled container comprising:

providing a container made of a composition comprising a polyolefin material and a radiation stabilizer;

filling the container with a medium; and

irradiating said container filled with said medium with gamma radiation, wherein said medium includes less than about 3.4 ppm of oxidizable substances after said irradiating step.

18. A method as in claim 17, further comprising a step of sealing the container after filling the container with the medium and prior to irradiating the container.

19. A method as in claim 18, further comprising a step of enclosing the container within packaging after sealing the container, and wherein the irradiating step comprises irradiating said container within said packaging.

20. A method as in claim 19, wherein said packaging comprises a blister package.

21. A method as in claim 17, wherein the medium is selected from the group consisting of a therapeutic fluid and a non-therapeutic fluid.

22. A method as in claim 17, wherein the medium comprises a drug for parenteral administration to the body.

23. A method as in claim 17, wherein the medium comprises a saline water.

24. A method as in claim 17, wherein the gamma radiation is in a range from about 10 kGy to about 60 kGy.

25. A method as in claim 17, wherein the container is manufactured from a composition comprising a polyolefin, a mobilizing amount of a liquid mobilizer compatible with said polyolefin, and a radiation stabilizing amount of a hindered piperidine stabilizer.

26. A method as in claim 25, wherein the container further comprises a clarifying amount of a dibenzylidene sorbitol alkyl thioether clarifier.

27. A method as in claim 25, wherein the container further comprises a nucleating agent comprising a 2,2'-methylene-bis(4,6-di-t-butylphenol)phosphate salt.

28. A method as in claim 25, wherein the composition of the container further comprises about 0.1 to 10% of an additional polymer.

29. A method as in claim 25, wherein the polyolefin is selected from the group consisting of polyethylene, polypropylene, polymethylpentene, polytetrafluoroethylene and copolymers thereof.

30. A method as in claim 25, wherein the container comprises a bag for intravenous fluid delivery.

31. A method as in claim 25, wherein the container comprises a syringe.

32. A sterilized article comprising:

a container made of a composition comprising a polyolefin material and a radiation stabilizer; and

a medium contained within said container, said medium including less than about 3.4 ppm of oxidizable substances,

wherein said container containing said medium therein has been subjected to a gamma irradiation sterilization treatment after being filled with said medium.

33. A sterilized article as in claim 32, wherein the medium is selected from the group consisting of a therapeutic fluid and a non-therapeutic fluid.

34. A sterilized article as in claim 32, wherein the medium contained within the container comprises a drug for parenteral administration to the body.

35. A sterilized article as in claim 32, wherein the medium comprises saline water.

36. A sterilized article as in claim 32, wherein the container comprises a bag for intravenous fluid delivery.

37. A sterilized article as in claim 32, wherein the container comprises a syringe.

38. A sterilized article as in claim 32, wherein the container is manufactured from a composition comprising a polyolefin, a mobilizing amount of a liquid mobilizer compatible with said polyolefin, and a radiation stabilizing amount of a hindered piperidine stabilizer.

39. A sterilized article as in claim 38, wherein the container further comprises a clarifying amount of a dibenzylidene sorbitol alkyl thioether clarifier.

40. A sterilized article as in claim 38, wherein the container further comprises a nucleating agent comprising a 2,2'-methylene-bis(4,6-di-t-butylphenol)phosphate salt.

41. A sterilized article as in claim 40, wherein the 2,2'-methylene-bis(4,6-di-t-butylphenol)phosphate salt is selected from the group consisting of sodium 2,2'-methylene-bis(4,6-di-t-butylphenol)phosphate and aluminum 2,2'-methylene-bis(4,6-di-t-butylphenol)phosphate.

42. A sterilized article as in claim 38, wherein the composition of the container further comprises about 0.1 to 10% of an additional polymer.

43. A sterilized article as in claim 38, wherein the polyolefin is selected from the group consisting of polyethylene, polypropylene, polymethylpentene, polytetrafluoroethylene and copolymers thereof.

44. A sterilized article as in claim 38, wherein the mobilizing additive is selected from the group consisting of a hydrocarbon oil, phthalic ester oil, polymer grease, vegetable oil, mineral oil and silicone oil.

45. A sterilized article as in claim 38, wherein the stabilizer is a bis(4-piperidinyl) diester of a dicarboxylic acid.

46. A method as in claim 1, wherein the radiation stabilizer comprises a liquid mobilizer compatible with said polyolefin.

47. A method as in claim 1, wherein the radiation stabilizer comprises a hindered amine stabilizer.

48. A method as in claim 17, wherein the radiation stabilizer comprises a liquid mobilizer compatible with said polyolefin.

49. A method as in claim 17, wherein the radiation stabilizer comprises a hindered amine stabilizer.

50. A sterilized article as in claim 32, wherein the radiation stabilizer comprises a liquid mobilizer compatible with said polyolefin.

51. A sterilized article as in claim 32, wherein the radiation stabilizer comprises a hindered amine stabilizer.

52. A method as in claim 1, wherein the oxidizable substance is hydrogen peroxide.

53. (Cancelled)

54. A method as in claim 17, wherein the oxidizable substance is hydrogen peroxide.

55. A sterilized article comprising:

a container; and

a medium contained within said container,

wherein said container containing said medium therein has been subjected to a gamma irradiation sterilization treatment after being filled with said medium, and wherein the medium includes less than about 3.4 ppm of oxidizable substances after said irradiating step.

56. A method as in claim 32, wherein the oxidizable substance is hydrogen peroxide.

(ix) EVIDENCE APPENDIX

None.

(x) RELATED PROCEEDINGS APPENDIX

None.